The American Journal of Medicine (2005) 118, 565–568

ELSEVIER

THE AMERICAN JOURNAL *of* MEDICINE®

LETTERS

Is life expectancy of polycythemia vera patients clearly different from that of the general population?

To the Editor:

In a recent issue of the *American Journal of Medicine*, Passamonti et al reported a significantly higher mortality for polycythemia vera (PV) patients than in a sex-, age-, and calendar year-matched Italian general population in a retrospective analysis of 396 PV patients, using standardized mortality ratio (SMR).[1] Thrombosis was the most frequent complication and the main cause of death, and a history of thrombosis was the only adverse prognostic factor for survival. By contrast, survival of patients with essential thrombocythemia was similar to that of the general population.

We previously published the final analysis of a prospective study that enrolled 179 PV patients with the longest mean follow-up reported to date of 11.4 years.[2] In our study, SMR for the entire cohort, as well as for the different age and sex subgroups, were not statistically different from those of the French population. We also found that hyperleukocytosis was a significant risk factor for evolution to leukemia and shortened survival. A trend for such unfavorable impact of hyper leukocytosis on leukemic evolution ($P = 0.065$) was also reported in the recent analysis of the European Collaboration on Low-dose Aspirin in Polycythemia Vera (ECLAP) prospective study.[3]

Reaching a balance between the vascular risk and the possible leukemogenicity of cytoreductive treatments is a major aim in the therapeutic strategy of PV. Evaluation of life expectancy of PV patients, identification of prognostic factors, and precise determination of very long-term complications are crucial for the management of this long-lasting disease. In our study, the incidence of thrombosis (15% at 10 years) was even lower than observed in the French matched-control population, showing that a careful management of PV might reduce the vascular risk associated with the disease. All our patients had been homogeneously treated with a cytoreductive agent (pipobroman) with a very high response rate of 98%. In the Passamonti et al study, various therapeutic strategies were used and the response rate was not documented, making difficult the interpretation of the high incidence of thrombosis reported. Furthermore, the somewhat shorter follow-up (9.6 years versus 11.4 years in our study), the smaller number of deaths observed (33% compared to 54% in our study), and the retrospective nature of their study could have biased the data obtained.

Finally, controversies concerning outcome of patients with myeloproliferative disorders stress the need for long-term data obtained from prospective studies in chronic malignancies that cannot be cured with currently available drugs.

Jean-Jacques Kiladjian
Jean-Francois Bernard
Pierre Fenaux
Service d'Hematologie Clinique
Hopital Avicenne and Paris 13 University
Bobigny, France

doi:10.1016/j.amjmed.2004.12.026

References

1. Passamonti F, Rumi E, Pungolino E, et al. Life expectancy and prognostic factors for survival in patients with polycythemia vera and essential thrombocythemia. *Am J Med.* 2004;117:755–761.
2. Kiladjian JJ, Gardin C, Renoux M, Bruno F, Bernard JF. Long-term outcomes of polycythemia vera patients treated with pipobroman as initial therapy. *Hematol J.* 2003;4:198–207.
3. Finazzi G, Caruso V, Marchioli R, et al. Acute leukemia in polycythemia vera. An analysis of 1638 patients enrolled in a prospective observational study. *Blood.* 2005;105:2664-2670.

The Reply:

Kiladjian et al state that the results of their study showed a standardized mortality ratio (SMR) of 1.0 and a 15-year risk of thrombosis of 21.8% in 164 polycythemic patients.[1] In our cohort of 396 patients with polycythemia vera, SMR was 1.6 and the 15-year risk of thrombosis was 27%.[2]

The patient cohort included 130 patients with polycythemia vera and 34 individuals with idiopathic erythrocytosis. Idiopathic erythrocytosis represents a grey zone between diagnosis of polycythemia vera and that of secondary erythrocytosis.[3] The fact that 20% of patients in the Kiladjian study were classified as idiopathic erythrocytosis might explain the lower SMR and the slightly lower risk of thrombosis compared with our study that included only patients with polycythemia vera.

To estimate SMR, Kiladjian et al compared the observed mortality with the probability of death in an age- and sex-

0002-9343/$ -see front matter © 2005 Elsevier Inc. All rights reserved.

matched French population. Usually, SMR is calculated by applying the mortality rates (ie, the incidence of death), and not the probability of death, in the reference population in comparison with the study cohort. In contrast to the French study, we used age-, sex-, and calendar-year specific reference rates to calculate the SMR.[2] This allows for more reliable estimates especially when the cohort has a long period of recruitment, because mortality rates tend to vary with time.

Kiladjian et al also report an incidence of thromobosis even lower than that observed in the French matched-control population. This statement, however, is not supported by appropriate data because a direct comparison of the incidence of thrombosis between patients and the control population is not reported.

Finally, concerning the well-known potential biases of retrospective studies, in the cohort of 396 patients followed at our centres, the rate of patients lost to follow-up was as low as 2.5%, even lower than that reported by the prospective study by Kiladjian et al (11.6%).

Francesco Passamonti, MD
Mario Cazzola, MD
Mario Lazzarino, MD
Division of Hematology, IRCCS Policlinico San Matteo University of Pavia, Pavia, Italy

Enrica Morra, MD
Division of Hematology, Niguarda Cà Granda Hospital Milan, Italy

doi:10.1016/j.amjmed.2005.01.057

References

1. Kiladjian JJ, Gardin C, Renoux M, et al. Long-term outcomes of polycythemia vera patients treated with pipobroman as initial therapy. *Hematol J*. 2003;4:198–207.
2. Passamonti F, Rumi E, Pungolino E, et al. Life expectancy and prognostic factors for survival in patients with polycythemia vera and essential thrombocythemia. *Am J Med*. 2004;117:755–761.
3. Blacklock HA, Royle GA. Idiopathic erythrocytosis–a declining entity. *Br J Haematol*. 2001;115:774–781.

Regarding the Lakkireddy et al article on death certificate completion

To the Editor:

I read with interest the article on death certificate completion by Lakkireddy and colleagues.[1] We agree that guidance on the appropriate completion of death certificates receives little attention and that not only the range of quality but, as importantly, the degree of accuracy (which is used for many public health matters) is suboptimal.

We at the University of Florida Department of Medicine and adjacent VA Medical Center hold a monthly 1-hour session with the fellows in a program called ACCESS (Access and Continuity in the Education of Specialists). This program is meant primarily to continue the general internal medicine interests of fellows while they are in their fellowship. During the session, we review pertinent articles on all of medicine, professionalism, legal and ethical matters, as well as articles such as this one.

I prepared another case very similar to that of Lakkireddy et al, attempting to match that case's complexity and multisystem involvement. We used a scoring system based at 1 to represent a perfect or near-perfect completion of the death certificate, a score of 2 for almost perfect, 3 for an inaccurate but acceptable completion, and grade 4 for unacceptable, with the essential criterion for unacceptability being the cause of death listed as "cardiac arrest" or "arrhythmia."

When the case used by Lakkireddy et al was presented, the average score for PGY-4s (n = 9) was 2.8; the average score for the PGY-5s (n = 9) was 3.1; and the average score for PGY-6s/7s (n = 6) was 2.0. That session was immediately followed by a 30-minute discussion of the article in detail. Following that, my new case was presented for the remaining 15 minutes and the scores for the PGY-4s, PGY-5s, PGY-6/7s respectively improved to 1.7, 1.4, and 1.5. Perhaps more importantly for the group, the total percentage of optimal completion of death certificates increased from 17% before the lecture to 50% following the lecture, while the total number of unacceptable grade 4 completions dropped from 42% to 0%. The grade for the entire group before the lecture was 2.7, while the grade after this brief teaching exercise was 1.5. In discussion, the house staff agreed that more attention needed to be directed to correct completion of the cause of death and not to the mechanism of death.

This short exercise suffered from the involvement of a fairly small group (n = 24 fellows) and because only a brief single teaching program was offered. It also suffered from the assumption that the two cases were of equal complexity. Despite these criticisms, it does show that 1 hour of presentation with a pre- and postpresentation exercise can improve the quality of the death certificate as a usable instrument. Our findings are compatible with the assumptions made by Lakkireddy et al and demonstrate that even minimal effort can achieve improvement in this area.

Craig S. Kitchens, MD
Professor of Medicine
University of Florida
ACOS(E), VA Medical Center
Gainesville, Florida
Craig.kitchens.med.va.gov

doi:10.1016/j.amjmed.2004.11.024

Reference

1. Lakkireddy DR, Gowda MJ, Murray CW, et al. Death certificate completion: how well are physicians trained and are cardiovascular causes overstated? *Am J Med*. 2004;117:492–498.